

WE CLAIM:

1. An isolated and purified hFAST-1 protein comprising the amino acid sequence shown in SEQ ID NO:2 and naturally occurring biologically active variants thereof.

5 2. A fusion protein which comprises a first protein segment and a second protein segment fused to each other by means of a peptide bond, wherein the first protein segment consists of at least thirteen contiguous amino acids selected from the amino acid sequence shown in SEQ ID NO:2.

10 3. An isolated and purified polypeptide which consists of at least thirteen contiguous amino acids of hFAST-1 as shown in SEQ ID NO:2.

4. The isolated and purified polypeptide of claim 3 which binds to a Smad2 protein as shown in SEQ ID NO:3.

15 5. The isolated polypeptide of claim 3 wherein the at least thirteen contiguous amino acids of hFAST-1 comprise amino acids 277-364 of SEQ ID NO:2.

6. The isolated polypeptide of claim 3 wherein the at least thirteen contiguous amino acids of hFAST-1 comprise amino acids 221-365 of SEQ ID NO:2.

20 7. A preparation of antibodies which specifically bind to an hFAST-1 protein as shown in SEQ ID NO:2.

8. The preparation of antibodies of claim 7 wherein the antibodies are monoclonal.

9. The preparation of antibodies of claim 7 wherein the antibodies are purified from an animal antiserum.

25 10. The preparation of antibodies of claim 7 wherein the antibodies are affinity purified.

11. A subgenomic polynucleotide which encodes an hFAST-1 protein as shown in SEQ ID NO:2.

12. The subgenomic polynucleotide of claim 11 which is intron-free.

30 13. The subgenomic polynucleotide of claim 11 which comprises the sequence shown in SEQ ID NO:1.

14. A vector comprising the polynucleotide of claim 11. 15.

A vector comprising the polynucleotide of claim 12.

16. A vector comprising the polynucleotide of claim 13.

17. A recombinant host cell which comprises the polynucleotide of claim

5 11.

18. A recombinant host cell which comprises the polynucleotide of claim

12.

19. A recombinant host cell which comprises the polynucleotide of claim

13.

10 20. A recombinant DNA construct for expressing *hFAST-1* antisense
nucleic acids, comprising:

a promoter; and

a coding sequence for *hFAST-1* consisting of at least 12 contiguous
base pairs selected from SEQ ID NO:1, wherein the coding sequence is in an
15 inverted orientation with respect to the promoter, such that upon transcription
from said promoter an RNA is produced which is complementary to native mRNA
encoding *hFAST-1*.

21. The construct of claim 20 further comprising a transcription
terminator, wherein the coding sequence is between the promoter and the
20 terminator.

22. A method of screening test compounds for those which inhibit the
action of TGF- β , comprising the steps of:

contacting a test compound with a first protein which is all or a
portion of a Smad2 protein or a naturally occurring biologically active variant
25 thereof, wherein the portion of the Smad2 protein is capable of binding to *hFAST-1*,
and a second protein which is all or a portion of *hFAST-1* or a naturally
occurring biologically active variant thereof, wherein the portion of *hFAST-1* is
capable of binding to the portion of the Smad2 protein; and

determining an amount selected from the group consisting of: (a) the
30 first protein bound to the second protein, (b) the second protein bound to the first
protein, (c) the first protein which is not bound to the second protein, and (d) the

second protein which is not bound to the first protein, wherein a test compound which decreases the amount of (a) or (b) or increases the amount of (c) or (d) is a candidate compound for inhibiting the action of TGF- β .

5 23. The method of claim 22 wherein the step of contacting is performed *in vitro*.

24. The method of claim 22 wherein the step of contacting is performed by contacting a test compound with a cell which expresses the first protein and the second protein.

10 25. The method of claim 23 wherein the test compound is contacted with one of the two proteins prior to contacting with the other protein.

26. The method of claim 23 wherein one of the two proteins is bound to a solid support.

27. The method of claim 23 wherein at least one of the two proteins is radiolabeled.

15 28. The method of claim 23 wherein at least one of the two proteins is a fusion protein.

29. The method of claim 23 wherein at least one of the two proteins is a fusion protein that has a detectable enzyme activity.

20 30. A method of screening test compounds for the ability to decrease or augment TGF- β activity, comprising the steps of:

(a) contacting a cell with a test compound, wherein the cell comprises:

25 i) a first fusion protein comprising (1) a DNA binding domain or a transcriptional activating domain and (2) all or a portion of an hFAST-1 protein, wherein the portion consists of a contiguous sequence of amino acids selected from the amino acid sequence shown in SEQ ID NO:2, wherein the portion is capable of binding to Smad2 protein;

30 ii) a second fusion protein comprising (1) a DNA binding domain or a transcriptional activating domain and (2) all or a portion of Smad2 protein, or a naturally occurring

biologically active variant thereof, wherein the portion is capable of binding to hFAST-1 protein, wherein when the first fusion protein comprises a DNA binding domain, the second fusion protein comprises a transcriptional activating domain, and when the first fusion protein comprises a transcriptional activating domain, the second fusion protein comprises a DNA binding domain, wherein the interaction of the portion of the hFAST-1 protein with the portion of Smad2 protein reconstitutes a sequence-specific transcriptional activating factor;

iii) a reporter gene comprising a DNA sequence to which the DNA binding domain of the first or second fusion protein specifically binds; and

iv) hSmad4 protein; and

(b) measuring the expression of the reporter gene, a test compound which increases the expression of the reporter gene being a potential drug for increasing TGF- β activity, and a test compound which decreases the expression of the reporter gene being a potential drug for decreasing TGF- β activity.

31. A method of screening for drugs with the ability to decrease or augment TGF- β activity comprising the steps of:

(a) contacting a cell with a test compound and with TGF- β , wherein the cell comprises:

(i) all or a portion of Smad2 protein or a naturally occurring biologically active variant thereof, wherein the portion of Smad2 protein is capable of binding to hFAST-1;

(ii) all or a portion of hFAST-1 or a naturally occurring biologically active variant thereof, wherein the portion of hFAST-1 is capable of binding to Smad2 protein;

(iii) a vector which comprises a reporter gene under the control of an activin response element, wherein the activin response element comprises an hFAST-1 binding

motif TGT(G/T)(T/G)ATT as shown in SEQ ID NO:4; and

(iv) hSmad 4 protein; and

(b) measuring transcription of the reporter gene, a test compound which increases the amount of reporter gene transcription being a potential drug for augmenting TGF- β activity, and a test compound which decreases the amount of reporter gene transcription being a potential drug for decreasing TGF- β activity.

32. A recombinant construct which comprises a reporter gene under the control of an activin response element, wherein the activin response element comprises an hFAST-1 binding motif TGT(G/T)(T/G)ATT as shown in SEQ ID NO:4.

33. The recombinant construct of claim 32 wherein the construct comprises a vector.

34. The recombinant construct of claim 32 wherein the reporter gene encodes a non-human protein.

35. The recombinant construct of claim 34 wherein the non-human protein is selected from the group consisting of green fluorescent protein (GFP), luciferase, chloramphenicol acetyltransferase, and β -galactosidase.

36. A double-stranded DNA fragment which comprises an activin response element which comprises an hFAST-1 binding motif TGT(G/T)(T/G)ATT as shown in SEQ ID NO:4, wherein the fragment is covalently attached to an insoluble polymeric support.

37. An isolated and purified oligonucleotide which encodes at least thirteen contiguous amino acids of hFAST-1 protein as shown in SEQ ID NO:2.

38. An isolated and purified oligonucleotide which comprises at least 19 contiguous nucleotides of hFAST-1 as shown in SEQ ID NO:1.

39. The isolated oligonucleotide of claim 38 which is radiolabeled.

40. The isolated oligonucleotide of claim 38 which is fluorescently labeled.

41. The isolated oligonucleotide of claim 38 which comprises a sense strand.

42. The isolated oligonucleotide of claim 38 which comprises an antisense strand.

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